#38 The influence of cabergoline on the offspring phenotype of human chorionic gonadotropin (hCG)- secreting female mice: does mother's milk make the difference?

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Transgenic female mice expressing human chorionic gonadotropin-ß (hCGß+) produce elevated levels of hCG, prolactin and progesterone, show precocious puberty, are infertile and develop pituitary tumors. We have previously demonstrated that a short-term treatment of juvenile hCGß+ females with the dopamine agonist cabergoline normalizes the phenotypic changes of hCGß+ females. Even more, the treatment prevented phenotypic alterations on the transgenic offspring. The aim of this study was to determine if the cabergoline treatment has its effect during pregnancy and/or lactation. Two groups of 2-month-old wild-type (WT) females were mated with hCGß+ males: (1) Six-week-old WT females pretreated with cabergoline (500 µg/kg, ip), every other day for one week (WT-CAB mothers); (2) WT females without treatment (WT- mothers). Offspring from each mother was exchanged at birth and analyzed at three weeks of age. Transgenic offspring from WT-CAB mothers that ingested milk from WT mothers showed phenotypic alterations as exhibited in hCGß+ females, in terms of vaginal opening and increased uterus weight, as indicators of precocious puberty. On the other hand, the phenotype of transgenic offspring from WT mothers that received milk from WT-CAB mothers was normalized in terms of vaginal opening, uterus weight and ovarian gene expression of Lhcgr, Cyp11a1, Cyp17a1 and Cyp19a1 (qPCR). To analyze if the milk makes the difference, another group of WT females previously mated with hCGß+ males was treated with cabergoline during lactation from day 1 after birth for one week (0.1 µg/kg ip, every other day). Female transgenic offspring also showed a normalized phenotype at 3 weeks of age. These results suggest that cabergoline has an impact on the offspring during the lactating period and protects them from the phenotypic alterations induced by hCG hypersecretion. The molecular mechanisms involved in this phenomenon remain to be investigated.

#41 *In vivo* evaluation of estrogenic effects of dietary supplement Hops

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Hops is used as a suspected safe alternative to hormone replacement therapy for menopausal symptoms relief. Hops contains, among others, the phytoestrogen 8-prenylnaringenin (8-PN) and xantohumol (XN), which can be metabolized to 8-PN. XN acts as a cancer chemopreventive agent.

We aimed to evaluate the estrogenic properties of hops and knockout hops (KO-hops) (reduced in XN and consequently in 8-PN) using the uterotrophic assay.

Seven weeks old female Wistar rats were bilaterally ovariectomized. After fourteen days, rats were treated for three days with 17ß-estradiol (E2: 4 µg/kg bw/day) or fed with the vehicle (CON), hops or KO-hops at 8, 40 and 200 mg/kg bw/day. Animals were sacrificed 24 h after the last treatment day. The uterus was removed, weighed and processed for histology and mRNA extraction.

As expected, the relative uterine weight (rUW) and luminal epithelial cell height (LECH) were increased by the positive control E2 respect to CON ($p < 0.05$). The rUW was similar between hops, KO-hops and CON groups. An increase in LECH was shown in hops40 compared to CON ($p < 0.05$). E2 and KO-hops8 induced cell proliferation in the luminal epithelium compared to CON ($p < 0.05$). The mRNA expression of estrogen receptor a (Esr1) and complement C3 (C3) was downregulated and upregulated, respectively by E2 treatment ($p < 0.05$). Esr1 and C3